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# Blue-ringed octopuses: a brief review of their toxicology

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## Abstract

Blue-ringed octopuses *Hapalochlaena* (Cephalopoda: Octopoda: Octopodidae) live in shallow waters on rocky reefs in the intertidal and subtidal zones along the Australian coast. Their toxic saliva (venom) is used to subdue their prey of principally small crabs. The predominant toxin found in the saliva is tetrodotoxin (TTX), a sodium channel blocking neurotoxin, which causes dose-dependent muscle paralysis. The somewhat elusive Northern Australian Greater Blue-ringed Octopus *Hapalochlaena* sp. 1 is attributed to the first documented human fatality (at East Point, Dawin, in 1954) from a blue-ringed octopus; however the octopus was not correctly identified until 1964. This paper clarifies the first documented fatality from a blue-ringed octopus envenoming and briefly reviews the literature on the natural history and toxicology of blue-ringed octopuses, focusing on the Northern Australian Greater Blue-ringed Octopus, the only species of *Hapalochlaena* in the Northern Territory.

## Introduction

The genus *Hapalochlaena* comprises the blue-ringed octopuses, which are found along the entire Australian coast (Sutherland & Tibballs 2001). They frequent shallow rocky reefs in the intertidal and subtidal zones, avoiding surf conditions. At rest, the body of blue-ringed octopuses is a mottle of yellow to brown or grey with the defining blue rings blended into the brown-grey patches. Octopuses have the ability to darken and lighten patches to adapt to surroundings and assist with camouflage (Williamson 1996). Blue-ringed octopuses have additional powers of command over their skin pigmentation: their characteristic iridescent blue markings fluoresce when distressed or when desired (Hanlon & Hixon 1980; Hanlon 2007). There remains some uncertainty in the taxonomy of *Hapalochlaena* from northern Australia and in octopuses in general (see Willan 2008).

Following a sighting of the Northern Australian Greater Blue-ringed Octopus *Hapalochlaena* sp. 1 in the shallows of a muddy reef off East Point, Darwin, on a low tide midnight 18-19th May 2007 NT Field Naturalists' field trip, interest was sparked in this small, seemingly innocuous, yet highly dangerous sea creature. There are no data available on the abundance or distribution of this undescribed species within the Darwin coastal region. Marine biologists from Darwin estimate that while known to be common, they are rarely sighted (M. Meekan, pers. comm.). Of additional local importance, is the historical link with the first fatal envenoming from a Northern Australian Greater Blue-ringed Octopus, which also occurred off East Point, although the species of octopus responsible for the fatality was not confirmed until many years later. Members of the genus *Hapalochlaena* are the only octopuses known to be capable of causing toxic morbidity or mortality in humans (Meier 1995). This paper briefly reviews the natural history and toxicology of blue-ringed octopuses and clarifies details of the first documented fatality from envenoming by a Northern Australian Greater Blue-ringed Octopus in Darwin Harbour.

## Taxonomy and distribution

There are many species of *Hapalochlaena* of which three from Australia are broadly characterised as follows:

*Hapalochlaena maculosa* – Southern or Lesser Blue-ringed Octopus. Maximum size 20 cm across arms, body length 12 cm (Sutherland & Tibballs 2001); occurs along the coastline of south Western Australia to eastern Victoria, including Tasmania.

*Hapalochlaena fasciata* – Differs from *H. maculosa* in the appearance of blue rings, which appear as lines, instead of rings on the body; occurs chiefly along the coastline of eastern Australia to Victoria (Sutherland & Tibballs 2001).

*Hapalochlaena* sp. 1 – Northern Australian Greater Blue-ringed Octopus. Previously known under the name *H. lunulata*, which is restricted to tropical western Pacific Ocean including Papua New Guinea, Solomon Islands, the Philippines and Indonesia (see Willan 2008 for nomenclature). Slightly larger than *H. maculosa*; occurs along the coastline of Northern Australia.

## Life cycle and diet

Most species of blue-ringed octopuses live less than two years, reaching sexual maturity at four months (Tranter & Augustine 1973). The newly hatched juveniles feed on the yolk sac until about four weeks of age when as juveniles they begin attacking live crabs. Observational studies indicate that venom is active even at this early age (Tranter & Augustine 1973).

Octopuses possesses two sets of salivary glands; the larger set contains the potent tetrodotoxin (TTX)-like venom (Williamson 1996). *Hapalochlaena* use their poison to subdue their prey, predominantly crabs (Tranter & Augustine 1973; Walker 1983), but the method of attack depends on food availability. When food is plentiful, the octopus moves over its prey and disperses its toxic saliva into the surrounding water (Tranter & Augustine 1973; Walker 1983), the victim absorbs or inhales the venom and is paralysed within minutes (Tranter & Augustine 1973; Walker 1983). However, when starved, the octopus will actively capture prey with its arms and puncture its victim's shell with its beak, paralyzing it rapidly (Tranter & Augustine 1973; Walker 1983).

## Toxins

There remains some confusion concerning the precise molecular and toxinological differences between the structually similar organic compounds maculotoxin, derived from *Hapalochlaena maculosa*, and TTX, derived from pufferfishes. Some authors have classified any 'non-pufferfish'-derived tetrodotoxin to be TTX-like (Freeman & Turner 1970), while others claim they are pharmacologically and biochemically indistinguishable (Freeman 1976; Sutherland & Broad 1978), with the same chemical formula $C_{11}H_{17}N_3O_8$ (Kao 1972). Sutherland highlighted the complexity of the saliva and described the potential toxins contained in the posterior salivary glands of *H. maculosa* as follows: (a) tetrodotoxin-like substances (maculotoxin); (b) hapalotoxin; (c) antigenic, non-toxic components; (d) histamine, tyramine, serotonin and other phenolic amines; and (f) a potent hyaluronidase (suggested to be a dispersion agent) (Williamson 1996). Regardless of the names and possible molecular variations, TTX and maculotoxin ultimately have very similar and possibly identical clinical effects and outcomes (Mebs 2002).

TTX was named after the family of pufferfish the Tetraodontidae (four tooths) from which it was first isolated and purified in 1964 (Williamson 1996). Commonly eaten in South-east Asia as a delicacy called 'fugu' (Isbister *et al.* 2002), a miniscule portion of a poisonous organ from pufferfish (liver, ovaries, skin) can cause a tingling of the lips together with a lingering excitement that each bite is potentially a gamble with death. Too much TTX, a dose-dependent toxin, exclusively blocks nerve conduction by reducing the movement of sodium through membrane channels. This causes paralysis of muscles including the diaphragm, leading to respiratory failure and death (Mills & Passmore 1988; Williamson 1996; Isbister *et al.* 2002). TTX/maculotoxin has been isolated from all body parts of *H. maculosa* not just the posterior salivary gland, with high concentrations in the arms followed by the abdomen (Yotsu-Yamashita *et al.* 2007a). As in pufferfish, bacteria are thought to be responsible for the manufacture of TTX in *Hapalochlaena* (Hwang *et al.* 1989; Yu *et al.* 2004), possibly acquired through ingestion (Mills & Passmore 1988). Both pufferfish and newts bred in captivity do not acquire TTX (Mills & Passmore 1988).

TTX is widespread in nature. It has been identified in animals from six different major groups including pufferfish (Mills & Passmore 1988), central American frogs and newts (Yotsu-Yamashita *et al.* 2007b), goby fish (Hashimoto & Noguchi 1971), xanthid and horse-shoe crabs (Kanchanapongkul *et al.* 1996; Llewellyn *et al.* 2002), the gastropod *Nassarius glans* (Yin *et al.* 2005) and octopuses (Mills & Passmore 1988). Although TTX is thought to be produced by bacteria, the origins of these bacteria, their diversity in the natural world, how they disseminate and how frequently they can be taken up by animals remains unknown. It also remains to be elucidated as to whether TTX is found in other octopuses or other marine or terrestrial animals. Interestingly, saxitoxin (SXT) has recently been isolated in a species of octopus of the subgenus *Octopus* (*Abdopus*) (Robertson *et al.* 2004) from Port Hedland, Western Australia, and furthermore, homobatrachotoxin (homoBTX) has been found in the skin and feathers of birds of the genus *Pitohuis* from Papua New Guinea (Dumbacher *et al.* 1992; Dumbacher 1999). Further investigation of relationships between organisms and toxins in the food chain would help clarify the origins and potential distributions of these toxins in nature.

## Human envenoming and fatalities

Of all the octopuses, only *Hapalochlaena* is known to present an envenoming risk to humans (Sutherland & Tibballs 2001). Even so, blue-ringed octopuses are generally not aggressive to humans, biting only when provoked. In almost all recorded cases of envenoming, the octopus was clearly aggravated, such as by removal from the water. Furthermore, of the 12 documented bites by *Hapalochlaena*, six cases did not experience serious symptoms or deleterious respiratory consequences (Meier 1995). There have been two fatalities in Australia attributed to *Hapalochlaena*; the first in Darwin in 1954, and the second at Camp Cove near Sydney in 1967. Additionally, several envenomings have required life-preserving artificial ventilation until the neurotoxic effect of TTX had abated.

The bite of a blue-ringed octopus is often, but not always, painless and may go unnoticed (Flecker & Cotton 1955). Once envenomed, the toxin may advance rapidly, weakening and even paralysing the skeletal muscles of the victim. If the diaphragm is affected, respiratory failure and death may follow (Sutherland & Tibballs 2001). Dilated and unreactive pupils may be due to the toxin itself and not a true indication of cerebral dysfunction (Walker 1983). Victims usually remain mentally lucid and conscious throughout paralysis, with one report giving a terrifying account of hearing all that was said, including the statement "it looks as if this chap has had it" (Hopkins 1964). As there is no antidote to TTX, respiratory support together with reassurance may result in the victim surviving.

*The 1954 Northern Territory fatality*

The following is a summary of the first documented fatal envenoming from an octopus. It occurred off East Point beach, Darwin, on 19 October 1954 and was initially reported in the Medical Journal of Australia (Flecker & Cotton 1955). The victim, identified as 21 year old Kirke Dyson-Holland (Underhill 1996), a sailor and regular spear fisherman, was tossed a small octopus by his companion. Dyson-Holland placed the octopus on his shoulder while walking ashore. As he left the water, the octopus was thrown back into the water. A small trickle of blood was then noticed by his companion on the shoulder where the octopus had been. Shortly afterwards Dyson-Holland complained of dryness in the mouth and difficulty in breathing (Flecker & Cotton 1955). Initially he refused to see a doctor, but as his condition deteriorated he was rushed to the old Darwin hospital four miles (6.4 km) away at Myilly Point. During the trip he was heard to murmur "It was the little octopus, it was the little octopus" (Lane 1962). Upon arrival at hospital he was cyanosed (blue) and not breathing; despite respiratory assistance together with adrenaline, his heart stopped within 15 minutes of arriving at hospital. The time between octopus bite and death was estimated to be 90 minutes.

The victim was known to be asthmatic and the possibility of a hypersensitivity reaction was initially not ruled out. The octopus that caused the envenoming was thrown back into the sea, but later his diving companion produced an "identical" octopus which, although reported as being "iridescent blue", was incorrectly identified in the original Medical Journal of Australia article as *Octopus rugosus*, a much larger species of octopus which can cause local allergic effects similar to a bee sting (Flecker & Cotton 1955). However, this "identical" specimen was preserved and when re-examined many years later at the Australian Museum, Sydney, was found to be consistent with *Hapalochlaena* sp. 1 and not *O. rugosus* (McMichael 1964). The fatal clinical scenario described is consistent with classical TTX envenoming rather than asthma and/or an allergic reaction (Isbister *et al.* 2002).

McMichael (1961) recorded the effects of a bite from the Southern Blue-ringed Octopus (*Hapalochlaena maculosa*) from Wollongong, New South Wales, in 1950. At that time, he pointed out that the symptoms were very similar to those produced from cone snails *Conus* envenoming. McMichael (1964) subsequently identified a second octopus (also *Hapalochlaena maculosa*) responsible for the envenoming of a 33 year old man, who recovered with the aid of artificial respiration, in 1962 (Cleland & Southcott 1965; Sutherland & Tibballs 2001). An additional non-fatal envenoming occurred earlier in 1961 (Cleland & Southcott 1965; Sutherland & Tibballs 2001). Thus, by 1964 at least three documented envenomings but no deaths had occurred from the temperate Australian species *H. maculosa*. McMichael then reviewed and correctly identified the original preserved 1954 'identical' Darwin octopus, confirming that it was a blue-ringed octopus (McMichael 1964). Species in the genus *Hapalochlaena*

remain the only octopuses known to be potentially lethal, capable of causing toxic morbidity or mortality in humans (Meier 1995).

*The 1967 New South Wales fatality*

There has only been one other documented fatality from a blue-ringed octopus envenoming, which occurred in 1967 in New South Wales and was attributed to the Southern (or Lesser) Blue-ringed Octopus *Hapalochlaena maculosa*. A 23 year old army recruit found a purple octopus in a rock-pool near Sydney and placed it on the back of his hand. Within 10 minutes he complained of dizziness and the inability to remove the octopus. After a few minutes he could not swallow and was soon unable to breath. Mouth-to-mouth resuscitation was commenced together with cardiac massage. He was transferred to the nearest hospital, but despite further resuscitation attempts, he was declared dead approximately 90 minutes after initial contact with the octopus (Sutherland & Tibballs 2001; Meier 1995). The octopus was identified and reported by Lane and Sutherland (1967). This case confirmed that fatal neurotoxic envenoming can occur from bites from more than one of the *Hapalochlaena* species.

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The Northern Australian Greater Blue-ringed Octopus *Hapalochlaena* sp. 1, photographed at low tide on a reef at East Point, Darwin. (Bart Currie)